IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Kolter et al.	Docket No.:	51284
Serial No.:	09/811,546	Confirmation No.:	9100
Filing Date:	3/20/2001	Examiner:	SILVERMAN, ERIC E
Customer No.:	26474	Art Unit:	1615

For: Solid oral dosage forms with delayed release of active ingredient and high mechanical stability

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

REPLY BRIEF UNDER 37 C.F.R. §41.41

Sir:

This is a Reply Brief to the Examiner's Answer of November 29, 2007. Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account 14.1437. Please credit any excess fees to such account.

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Respectfully submitted,
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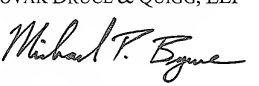

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STATUS OF CLAIMS

- Claims 1, 3 – 19 and 21 – 27 are currently pending.
- Claims 1, 3 – 19 and 21 – 24 stand rejected.
- Claims 2 and 20 are canceled.
- Claims 25 and 26 are withdrawn.
- Claims 1, 3 – 19 and 21 – 24 and 27 are being appealed.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the examiner erred in rejecting claims 1, 3 – 19, and 21 – 24 under 35 U.S.C. §103(a) over Kolter et al. (US 6,066,334) in view of Ortega (US 4,837,032).

ARGUMENTS

I. The results of the Examiner's proposed combination would not have been predictable to one of ordinary skill in the art.

In the case of *KSR International Co. v. Teleflex Inc.*,[1] the U.S. Supreme Court explained that "[i]f a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill."[2] Thus, it is clear, as expressed in the MPEP that "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art."[3]

According to the *Kolter et al.* reference, not only "[t]he amount and nature of the binder, but also the processing method, crucially influence the properties of solid presentations…."[4] The reference provides examples of the properties that are crucially influenced by the amount, the nature, and the processing method of the binder. The reference divides the properties that are crucially influenced into two categories: (1) properties of the granules, and (2) properties of compacts produced from the granules.

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[1] *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385 (2007).
[2] *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) (emphasis added).
[3] MPEP § 2143.01, subsection III.
[4] Column 1, lines 21 – 23 of US 6,066,334.

According to *Kolter et al.*, examples of the properties of the granules that would be crucially influenced by the Examiner's proposed combination include:

- particle size,
- flowability,
- compressibility,
- dust formation, and
- porosity or surface structure.

Examples of the properties of the compacts (produced from the granules) that would be crucially influenced by the Examiner's proposed combination include:

- breaking resistance,
- friability,
- disintegration, and
- release of the active ingredient.

A person of ordinary skill in the art at the time the present invention was made had no way to predict the extent or the nature of the crucial influence that the Examiner's proposed combination would have on these nine exemplary properties. Therefore, as a matter of law, the Examiner's suggestion that the proposed combination would have been obvious to a person of ordinary skill in the art is inadequate to establish a *prima facie* case of obviousness.

The only argument the Examiner has presented to the contrary is based on misconstruing column 2, lines 27 – 45 of *Kolter et al.* as a teaching that at concentrations in excess of 20% the disclosed polymer powders or granules "*might* alter the release rate"[5] of the active ingredient. First, this argument does not account for the other properties that would be crucially influenced by the Examiner's proposed combination. Second, this argument mischaracterizes the teaching of the *Kolter et al.* reference, which only addresses concentrations in the range of from 0.5 to 20% and does not provide a skilled artisan with a basis to speculate, let alone to predict, what properties might be influenced by deviation of the concentration to a percentage outside of the specified range.

[5] Page 4, lines 15 – 16 of the Examiner's Answer mailed November 29, 2007.

II. The Examiner's proposed combination would have required a change in the basic principle under which the primary reference was designed to operate.

In the case of *In re Ratti,*[6] The Court of Customs and Patent Appeals overturned an obviousness rejection based on a combination of references. The claimed invention was directed to a device that required resiliency for operation. The prior art described a device that required rigidity for operation. The Court ruled that the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] … was designed to operate."[7] Thus, it is clear, as expressed in the MPEP, that "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious."[8]

The *Kolter et al.* reference is generally directed to "the use of redispersible polymer powders or polymer granules … as binders for producing solid pharmaceutical presentations."[9] The reference stresses that its presentations "make rapid release of the active ingredients possible."[10] On the other hand, the present claims are directed to an oral dosage form with delayed release of active ingredient. Clearly, the Examiner's proposed combination would require a change in the basic principle under which the *Kolter et al.* reference was designed to operate.

The Examiner has attempted to avoid this issue by refusing to "afford patentable weight" to the phrase, "delayed release," because it is in the preamble of the claim. As already expressed, "clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention…."[11] Appellants have clearly relied on the preamble during prosecution to distinguish from the cited references, thus the examiner's refusal to "afford patentable

[6] *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).
[7] *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (CCPA 1959).
[8] MPEP § 2143.01, subsection VI.
[9] Column 1, lines 6 – 8 of US 6,066,334.
[10] Column 2, lines 20 – 22 of US 6,066,334 (emphasis added).
[11] *Catalina Mktg. Int'l v. Coolsavings.com, Inc.*, 289 F.3d at 808-09, 62 USPQ2d at 1785.

weight" to the phrase, "delayed release," is in error.

Of course, according to the Examiner, even if the preamble of claim 1 is *properly* given patentable weight, "the term 'delayed release' is not defined inasmuch as the disclosure does specify how much delay, if any, is required for the dosage form to be 'delayed release' as claimed."[12]

First, the specification makes clear that "delayed release" is far different than what is described in the *Kolter et al.* reference, because the present specification shows (1) that at most 25.3% of active ingredient is released after 1 hour,[13] and (2) that typically only 64.4% of active ingredient is released after 16 hours.[14]

Second, in reply to the Office action mailed on June 30, 2005, Appellants provided the Examiner with copies of the following references:

- Gundert-Remy et al. Oral Controlled Release Products Therapeutic and Biopharmaceutic Assessment, 1990, and
- USP 23 1880, General Information In Vitro and In Vivo Evaluation of Dosage Forms.

In these references, "delayed release" and "immediate release" are defined terms and are terms that one of ordinary skill in the art would well know and understand. Appellants also pointed to tables 2, 4 and 6 of the instant application wherein a time course of up to sixteen hours is required for a major portion of the active ingredients to be released, and argued that a release pattern such as disclosed in the instant invention falls well within the definition of "delayed release" as known to one of ordinary skill in the art.

III. The Examiner's proposed combination would render the *Kolter et al.* invention unsatisfactory for its intended purpose.

It is well-settled that a proposed modification to a prior art invention would not have been obvious, if it would render the prior art invention unsatisfactory for its intended purpose.[15] The *Kolter et al.* reference states that "[i]t is an object of the present invention to find polymer powders or polymer granules .... [which] make rapid release of

[12] Page 7, lines 7 – 9 of the Examiner's Answer mailed November 29, 2007.
[13] SEE: Table 12.
[14] SEE: Tables 2, 8 and 10.
[15] *See* MPEP §2143.01, citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

the active ingredients possible."[16] The claims also make clear that the active ingredient must be released within a time of from 0.1 to 1 hour, as measured in simulated gastric acid. The modifications proposed by the Examiner would render the *Kolter et al.* invention unsatisfactory for this purpose.

IV. In Conclusion

For at least these reasons, Appellants respectfully submit that the present rejection is in error and should be overturned. Favorable action is solicited.

[16] Column 2, lines 15 – 22 of US 6,066,334.